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Photolysis of 2-(Trifluoromethyl)quinoline 1-Oxides and 1-(Trifluoromethyl)isoquinoline 2-Oxide[1-3]

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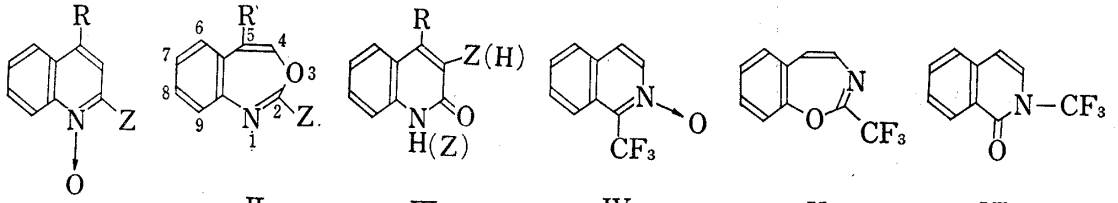
Photolysis of a series of 2-(trifluoromethyl)quinoline 1-oxides (1a—d) in various solvent is reported. In contrast to the large solvent effects upon the product distribution as found in the photolysis of quinoline 1-oxide and its 2-alkylated derivatives, the photolysis of these four N-oxides shows no such solvent effects and results in the formation of the corresponding 3,1-benzoxazepines (IIa—d), irrespective of the kinds of solvents used for irradiation. Similarly, the photolysis of 1-(trifluoromethyl)isoquinoline 2-oxide (IV) is also found to give the corresponding 1,3-benzoxazepine (V) as a sole rearrangement product.

A mechanistic rationalization of these photo-rearrangement reactions is presented.

The photochemistry of heteroaromatic amine oxides has been the subject of a number of recent publications.[5] A quinoline 1-oxide with either a hydrogen atom or an alkyl group in 2-position (I; Z=H, CH_3 *etc.*) apparently undergoes only two main types of rearrangement. In polar hydroxylic solvent the photo-product is 2-quinolone (III) and in non-polar, non-hydroxylic solvent the photo-product is predominantly 3,1-benzoxazepine (II).



I II III IV V VI

	Z	R
a	CF_3	H
b	CF_3	CH_3
c	CF_3	OCH_3
d	CF_3	CN

Chart 1

The substituent (especially the one attached to 2-position of the quinoline ring) also determines the course of the reactions. Thus, the ease of 2-quinolone formation over 3,1-

1) This forms Part XXIII of "Studies on the N-Oxides of π-Deficient N-Heteroaromatics," by C. Kaneko. For Part XXII, see C. Kaneko, H. Hasegawa, S. Tanaka, K. Sunayashiki, and S. Yamada, *Chemistry Letters*, **1974**, 133.
2) This forms also Part XV of "Studies on Organic Fluorine Compounds," by Y. Kobayashi. For Part XIV, see Y. Kobayashi, I. Kumadaki, Y. Hirose, and Y. Hanzawa, *J. Org. Chem.*, **39**, 1836 (1974).
3) Presented at the 89th Annual Meeting of Pharmaceutical Society of Japan, Nagoya, 1969. Preliminary Report, p. 173.
4) Location: *a) 2-3-10, Surugadai, Chiyoda-ku, Tokyo, 101, Japan; b) Kitashinjuku, 3-chome, Shinjuku-ku, Tokyo, 160, Japan.*
5) Recent reviews on this topic; *a)* C. Kaneko, *Kagaku no Ryoiki, Suppl.* **93**, 235 (1970); *b)* M. Ishikawa and C. Kaneko, *Kagaku no Ryoiki, Suppl.* **92**, 149 (1970); *c)* G.G. Spence, E.C. Taylor, and O. Buchardt, *Chem. Review*, **70**, 231 (1970); *d)* C. Kaneko, *Kagaku Sosetsu*, **1**, 131 (1973).

benzoxazepine formation decreases in the following order: quinoline 1-oxide, quinaldine 1-oxide, 2-phenylquinoline 1-oxide, 2-styrilquinoline 1-oxide, and 2-cyanoquinoline 1-oxide. The last two N-oxides (2-styril-[6] and 2-cyanoquinoline 1-oxides[7]) give only 3,1-benzoxazepine and no 2-quinolone is formed from these N-oxides even if irradiation is performed in methanol or ethanol. Isoquinoline 2-oxides have not been as fully investigated, but available results[5,8] indicate that similar processes take place.

As our further survey of the substituent effects existing in the photolysis of heteroaromatic amine oxides, we have irradiated the N-oxides of 2-(trifluoromethyl)quinolines (Ia—d) and 1-(trifluoromethyl)isoquinoline (IV). The present paper deals with the result and mechanistic rationalization, together with the structure determination and chemical reactions of the photo-products.

Result of Irradiation Experiments

Irradiation of 2-(trifluoromethyl)quinoline 1-oxide (Ia) and its 4-substituted derivatives (Ib—d) in ether gave the corresponding 3,1-benzoxazepines (IIa—d) in high yield (Table I).

Table I. Product Distribution of Photolyses of 2-(Trifluoromethyl)quinoline 1-Oxides (Ia—d) and 1-(Trifluoromethyl)isoquinoline 2-Oxide (IV)

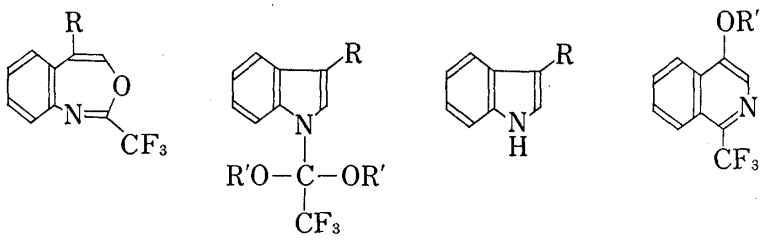
Quinoline 1-oxide	Solvent	Product (%)			
		Quinoline	3,1-Oxazepine (II)	Indole (VII)	Other (VII')
Ia (R=H)	ether	3—5	70	—	—
	CH_3OH	3—5	—	70	—
Ib (R=CH_3)	ether	3—5	50	—	—
	CH_3OH	3—5	—	30	10
Ic (R=OCH_3)	ether	2—5	65	—	—
Id (R=CN)	ether	3—5	75	—	—

Isoquinoline 2-oxide	Solvent	Product (%)		
		Isoquinoline	1,3-Oxazepine (V)	VIII
IV	ether	5	55	—
	CH_3OH[b]	5—7	—	11 (R'=CH_3)
	CH_3CH_2OH[b]	5—7	—	8 (R'=CH_2CH_3)

a) Irradiation was continued just until all of the N-oxide was consumed. Yields are given in weight % based on the starting N-oxide.
b) Several products were detected by TLC and GPC, but none of them could be purified.

The yield of 3,1-benzoxazepines did not change significantly when N-oxides were irradiated in acetone or benzene. However, if the N-oxides were irradiated in methanol or ethanol no benzoxazepine was detected and new products, derivatives of indole (VII and VII') appeared in the reaction mixture. As will be described later, all of these indoles were obtained by the solvolysis of the benzoxazepines with an alcoholic solvent at room temperature. These results provide a good supporting evidence for the formation of 3,1-benzoxazepines as primary photo-products irrespective of the kinds of solvent used for irradiation of the N-oxides (Ia—d).

6) I. Yokoe, M. Ishikawa, and C. Kaneko, *Rept. Res. Inst. Med. Engi., Tokyo Medico-Dental Univ.*, **6**, 18 (1972).
7) C. Kaneko and S. Yamada, *Chem. Pharm. Bull.* (Tokyo), **15**, 555 (1966).
8) C. Lohse, *J. Chem. Soc.*, **1972**, 229 and the references cited therein.



IIa—d VII VII' VIII

Chart 2

In all of these reactions, only other identified photo-products were the respective parent bases (2-(trifluoromethyl)quinolines (<10%)) and 2-quinolone derivatives were not detected.

Irradiation of 1-(trifluoromethyl)isoquinoline 2-oxide (IV) in ether or acetone also gave the corresponding 1,3-benzoxazepine (V) as a sole rearrangement product, together with a small amount of the parent amine. However, if irradiation was carried out in an alcoholic medium, the benzoxazepine was not detected and the new products (VIII: R'=CH_3 or CH_2-CH_3) were obtained, instead.

Though the insufficient amount of 1-(trifluoromethyl)isoquinoline 2-oxide (IV) prevented us from studying its photolysis in detail, it was assured by gas chromatographic analysis that the corresponding 1-isoquinolone (VI) was not formed even by irradiation in an alcoholic medium. This and the fact that the compounds (VIII) were not obtained in the solvolysis of the 1,3-benzoxazepine (V) with methanol or ethanol suggest not only that the primary photo-product is the 1,3-benzoxazepine (V), thereby proving there exist no first order solvent effects in the photolysis of IV, but also that the precursor of the products (VIII) cannot be the 1,3-benzoxazepine (V).

Discussions

The intervention of an oxaziridine intermediate has been suggested by us[5a,b,d] and others[5c] to explain the photochemical rearrangement reaction of heteroaromatic amine oxides. In the photolysis of quinoline 1-oxides, for example, the oxaziridine (IX) has been assumed to be formed in the primary step from the excited N-oxides.[9,10] In hydroxylic solvents, the next step involves the formation of the ion (X), followed by a [1,2] shift of the 2-substituent. In non-polar solvents, the pathway from oxaziridine (IX) is formulated as a [1,5]-suprafacial sigmatropic shift to the epoxy structure (XII) followed by a disrotatory ring opening to the 3,1-benzoxazepine (II). These two pathways (a and b) are depicted schematically in Chart 3.

In path a, we have assumed that the oxaziridine having either a hydrogen atom or an alkyl group would give 2-quinolone *via* π-complex (XI).[11] This tentative assumption seems to be now firmly verified by the selective formation of the 3,1-benzoxazepines (II) from Ia—d, because in a usual carbonium ion rearrangement reaction no example has been known in which a trichloro- or trifluoromethyl group migrates.[12,13]

9) M. Ishikawa, S. Yamada, and C. Kaneko, *Chem. Pharm. Bull.* (Tokyo), **13**, 747 (1965).

10) *a*) C. Kaneko, S. Yamada, I. Yokoe, and M. Ishikawa, *Tetrahedron Letters*, **1967**, 1873; *b*) C. Kaneko, S. Yamada, and I. Yokoe, *ibid.*, **1966**, 4701.

11) M. Ishikawa, C. Kaneko, I. Yokoe, and S. Yamada, *Tetrahedron*, **25**, 295 (1969) and references cited therein.

12) M.J.S. Dewar, "Molecular Rearrangements," edited by P. DeMayo, Vol. 1, Intersciencs Publishers, New York, 1963, p. 322.

13) In the π-complexes such as XI, the migrating group (Z) is held by a bond formed by the sharing of n electrons (n=2 or 6) between (n+1) atoms; here Z has a significant positive charge, regardless of any additional effects due to uneven sharing of electrons. Therefore, Z is more positive in the π-complex than in the isomeric classical structure, and so Z should migrate the more easily, the lower its affinity for electrons. Since the trihalomethyl groups have very high affinity for electrons, they should not migrate *via* π-complexes.

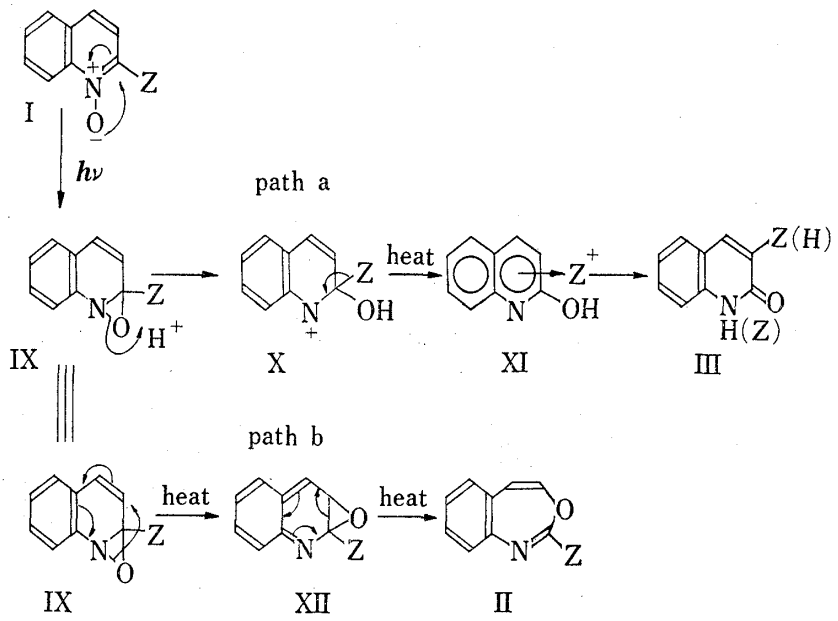


Chart 3

Complete lack of 1-isoquinolone formation in the photolysis of IV also indicates that path a in this and the related 2-oxide is an ionic process.

Thus, these results have provided an evidence strongly supporting our previously proposed mechanism for path a and excluded the possibility of intervention of a radical process which includes the homolytic fissions of N–O and C–Z bonds in an oxaziridine (*cf.* IX).[14]

Though the formation of an oxaziridine species from an excited heteroaromatic amine oxide has been explained reasonably by the use of MO theory,[15,16] the actual isolation of an oxaziridine has not been achieved as yet. However, the oxaziridine (IX: Z=CN) has been trapped by primary or secondary amines to give the corresponding 1-amino-carbostyrils in the photolysis of 2-cyanoquinoline 1-oxide[17] and the dibenz[*c*,*f*]-1,2-oxazepines (the valence bond tautomers of the corresponding oxaziridines) have been isolated as stable primary photo-

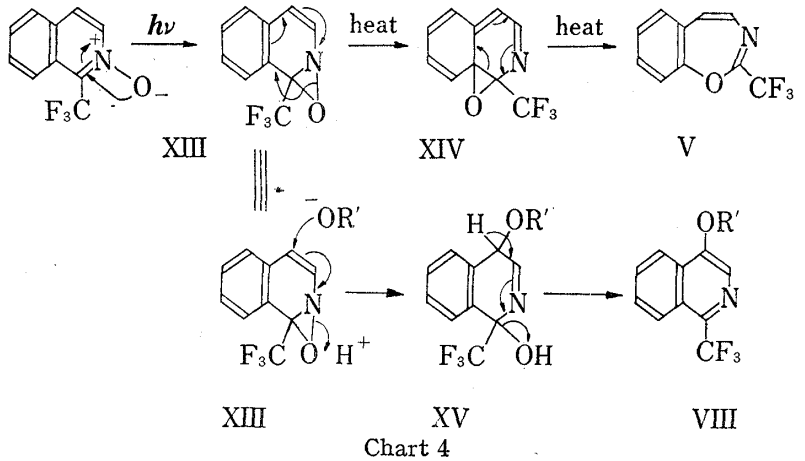


Chart 4

14) On the contrary, the photolysis of 2-halogenoquinoline 1-oxides resulted in the selective formation of 2-quinolones, irrespective of the kinds of solvents. An intervention of the radical fission process was suggested in these photolyses; I. Yokoe, M. Ishikawa, and C. Kaneko, in preparation.

15) *a*) C. Kaneko, S. Yamada, I. Yokoe, and T. Kubota, *Tetrahedron Letters*, **1970**, 2333; *b*) C. Kaneko, S. Yamada, H. Ichikawa, M. Yamakawa, and T. Kubota, Symposium on Photochemistry, Osaka, 1972. Abstract of papers, p. 159.

16) Y. Kobayashi, I. Kumadaki, and H. Sato, *Tetrahedron Letters*, **1970**, 2337.

17) C. Kaneko, I. Yokoe, and M. Ishikawa, *Tetrahedron Letters*, **1967**, 5237.

products in the photolysis of acridine 10-oxides.[18] In this connection, it is worthy to note that the isolation of 4-alkoxy-1-(trifluoromethyl)isoquinolines (VIII: R=CH_3 or CH_2CH_3) might be regarded as a first direct demonstration for the intermediary of an oxaziridine (XIII) in the photolysis of isoquinoline 2-oxide derivatives, because the oxaziridine is reasonably assumed to be a possible precursor of the product of VIII-type as shown in Chart 4.

This type of reaction has recently been observed in the photolysis of N-acylimino-isoquinolinium betaine in ethanol.[19]

Structure Determination and Chemical Reactions of the Photo-Products

The main photo-products in the photolysis in a non-hydroxylic solvent of 2-(trifluoromethyl)quinoline 1-oxides (Ia—d) are shown to be 2-(trifluoromethyl)-3,1-benzoxazepines (IIa) and its 5-substituted derivatives (IIb—d) by the presence of acceptable parent peaks in the mass spectra and from the other spectral data. By the same reasons, the photo-product in the photolysis of 1-(trifluoromethyl)isoquinoline 2-oxide (IV) in ether is also assigned to be 2-(trifluoromethyl)-1,3-benzoxazepine (V).

Their nuclear magnetic resonance (NMR) spectra are shown in Table II, which also contains those of the corresponding 2-cyano-3,1-benzoxazepine (IIe) and 2-cyano-1,3-benzoxazepine (XVI) obtained in our previous works.[7,20]

Table II. NMR Spectra of 3,1-Benzoxazepines (II) and 1,3-Benzoxazepines (V)

Benzoxazepine	$-CH_3$	Olefinic proton	
		H_4	H_5
IIe (R=H, Z=CN)	—	4.07, d (J=6)	4.28, d (J=6)
IIa (R=H, Z=CF_3)	—	4.03, d (J=6)	4.34, d (J=6)
IIb (R=CH_3, Z=CF_3)	8.10, d (J=2)	3.92, q (J=2)	—
IIc (R=OCH_3, Z=CF_3)	6.35, s	3.92, s	—
IId (R=CN, Z=CF_3)	—	3.75, s	—
2-Cyano-1,3-benzoxazepine (XVI)	—	3.32, d (J=8)	3.48, d (J=8)
V	—	3.22, d (J=8.5)	3.44, d (J=8.5)

All the spectra were recorded in $CDCl_3$ with TMS as internal standard. Chemical shifts are in τ-unit, coupling constants are in Hz.

The indoles (VIII': R=CH_3 and CN) are known compounds and were identified by the mixed melting point determination with the authentic specimen. The new indole derivatives (VII) were identified by elemental analysis and by comparison of their ultraviolet (UV) and NMR spectra with those of the previously described N-(1-cyano-1-dialkoxymethyl)indoles.[5a,b] By acid hydrolysis, these N-substituted indoles (VII) gave the corresponding parent indoles of the VII'-type.

The structures of 4-alkoxy-1-(trifluoromethyl)isoquinolines (VIII) were also deduced from their elemental analysis and from the acceptable UV and NMR spectra. The UV spectra of these two products resemble that of the parent isoquinoline and the NMR spectra show a sharp singlet due to the C_3-proton at τ 1.95 and a broad signal at about τ 1.8 due to the protons on C_5 and C_8, respectively. The large down-field shift of C_5-H signal in VIII from that of the parent 1-(trifluoromethyl)isoquinoline indicates clearly that the alkoxy group is introduced in the ring at C_4 position.

The 3,1-benzoxazepines (II) are led to a variety of indole compounds by hydrolysis. Thus, hydrolysis of IIa and IIb in boiling 50% aqueous ethanol containing 5% hydrochloric

18) S. Yamada, M. Ishikawa, and C. Kaneko, *Chem. Commun.*, **1972**, 1093. See also, S. Yamada, M. Ishikawa, and C. Kaneko, *Tetrahedron Letters*, **1972**, 971, 977.
19) Y. Tamura, S. Matsugashita, I. Ishibashi, and M. Ikeda, *Tetrahedron*, **29**, 2359 (1973).
20) C. Kaneko and S. Yamada, *Rept. Res. Inst. Med. Engi., Tokyo Medico-Dental Univ.*, **2**, 804 (1966).

acid resulted in the formation of indole or skatol (VII′: R=H or CH_3), respectively, in high yield, whereas solvolysis of these compounds in methanol or ethanol gave N-substituted indoles (VII) in predominant yield. By the same hydrolysis, however, IId gave only 3-cyanoindole (VII′: R=CN), presumably *via* the VII type compound.

The conversion of 3,1-benzoxazepines to indoles of VII- or VII′-type has many precedents and the mechanism has been previously discussed in detail.[5b,6,10b] Thus, the following pathways can be given for these solvolytic reactions (*cf.* Chart 5).

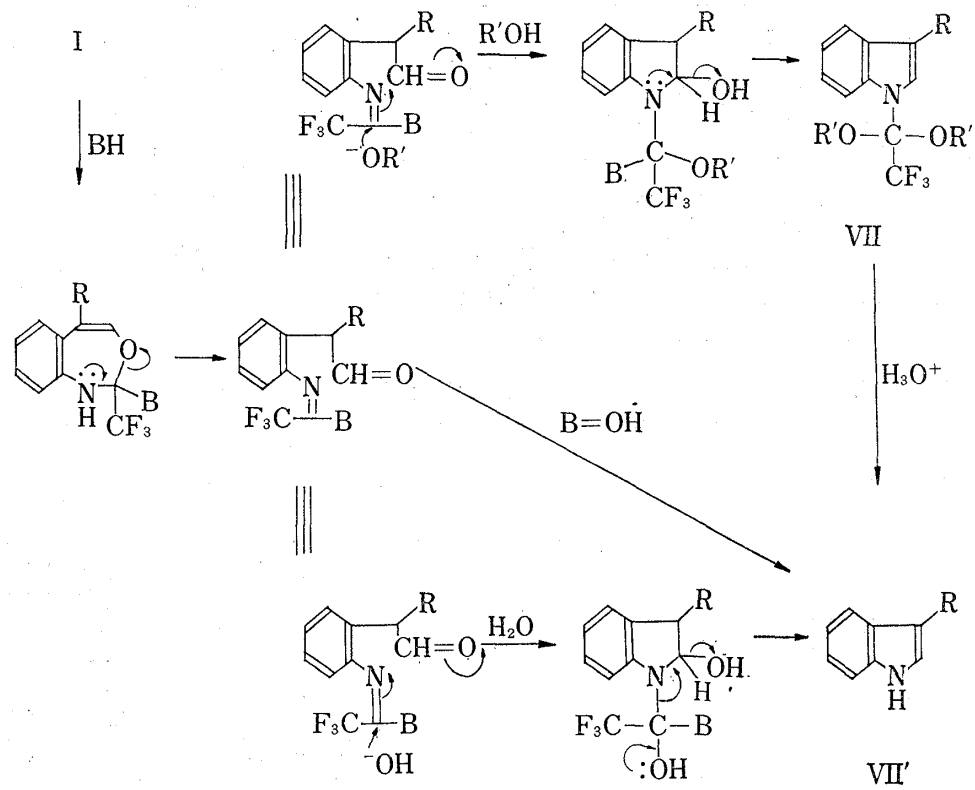


Chart 5

Since the same N-substituted indoles (VII) were also obtained as the photo-products from the irradiated solution of Ia or Ib in methanol or ethanol, it is obvious that the corresponding 3,1-benzoxazepines (IIa or IIb) are the direct primary photo-products in these irradiation experiments.

Very interestingly, the oxazepine (IIc), if boiled in methanol, gave rise to 4-methoxy-2-(trifluoromethyl)quinolin-3-ol (XVII) in addition to the usual solvolytic products (VIIc and VIIc′). In refluxed benzene, the yield of XVII was raised to 53% and a small amount of other phenolic product (XVIII) was also obtained. The combustion data and mass spectrum of XVIII agreed well with those of 2-(trifluoromethyl)quinolin-3,4-diol, but the definite structure determination must await further study.

The formation of XVII can reasonably be explained by assuming the corresponding 2,3-epoxyquinoline (*cf.* XII) as a key intermediate. Essentially the same rearrangement reactions have been found to occur in the reactions of 2-cyano-3,1-benzoxazepine derivatives in the presence of Lewis acid in an appropriate aprotic solvent.[21]

The 1,3-benzoxazepine (V) obtained from IV was also found to be highly reactive towards solvolytic reactions as reminiscent of 2-unsubstituted or 2-alkylated 1,3-benzoxazepines.[10b] However, due to insufficiency of IV (and therefore V), any of the solvolytic reaction products

21) S. Yamada and C. Kaneko, *Rept. Res. Inst. Med. Engi., Tokyo Medico-Dental Univ.*, 3, 75 (1969).

of V has not been identified from either the photochemical reaction mixture of IV or from the solvolytic reaction products of V in an alcoholic medium. However, since the pattern of gas chromatography was almost identical between the direct irradiation products of IV in methanol and methanol solution of V, except that the former contained an extra peak corresponding to 4-methoxy-1-(trifluoromethyl)isoquinoline, it seems obvious that here again the primary photo-product was the 1,3-benzoxazepine (V) irrespective of the kinds of solvents employed in the photolysis of IV. The fact that the product of the VIII-type compound was only isolated in the direct photolysis of IV in an alcoholic medium strongly suggests that the oxaziridine (XIII) was trapped by the alcohol as shown in Chart 4.

Experimental

The melting points were determined in a capillary tube and are uncorrected. The UV absorption spectra were measured on a Hitachi Model-323. The NMR spectra were obtained using a C-60 HL JEOL (60 Mcps) and the chemical shifts are in τ-units. The mass spectra were recorded on Hitachi Model-RMU-7M double focus mass spectrometer using in all cases a direct sample insertion into the ion source. All the new compounds described in this paper are supported either by satisfactory analytical results or by the presence of the corresponding parent peaks in the mass spectra.

Photolyses were carried out in an immersion apparatus equipped with 200 W Hanovia high pressure mercury lamp with a Pyrex filter and cooled internally with running water.

Quinoline N-Oxides (Ia—d)——All of the quinoline 1-oxides used in this study were prepared from the corresponding quinolines by the method of Ochiai using CF_3COOH instead of CH_3COOH.[22] The parent bases were prepared from the corresponding carboxylic acids by the method reported by one of the present authors (Y.K.).[23] Each N-oxide was characterized by satisfactory combustion, mass, and other spectral data, respectively, and has the following melting point: Ia, 100—101°; Ib, 154—155°; Ic, 136—137°; Id, 180—181°.

(Trifluoromethyl)isoquinoline 2-Oxide (IV)——To a solution of 1-(trifluoromethyl)isoquinoline (2 g) in CF_3COOH (5 ml), 30% H_2O_2 (1.5 ml) was added and the mixture was warmed at 60—65° on a water bath for 7 hr. The reaction mixture was concentrated *in vacuo* to about half the original volume and, after the same amount of water was added, the solution was concentrated to half the volume; the same procedure was repeated several times. Then the solution was made alkaline with solid Na_2CO_3 and extracted with $CHCl_3$. After the extract was dried over Na_2SO_4, the solvent was evaporated. The residue was recrystallized from isopropyl ether to give colorless needles of 1-(trifluoromethyl)isoquinoline 2-oxide, mp 85—87°. Yield, 0.8 g (38%). *Anal.* Calcd. for $C_{10}H_6ONF_3$: C, 56.36; H, 2.82; N, 6.57; F, 26.76. Found: C, 56.03; H, 2.97; N, 6.75; F, 27.34.

Irradiation of 2-(Trifluoromethyl)quinoline 1-Oxides (I) in Dry Ether——A 0.1% solution (w/v) of the N-oxide in an ether was irradiated in argon until the N-oxide had been consumed. In general, photolysis was complete in 60—90 min for 500 mg samples. Evaporation of the solvent *in vacuo* and repeated pentane extraction yielded the crude oxazepine (II). The results of irradiation experiments are shown in Table I.

Only IId was obtained in a crystalline form, mp 43—45° (from pentane). UV λ_{max}^{ether} mμ (log ε): 232 (4.32), 311 (3.24). *Anal.* Calcd. for $C_{11}H_5ON_2F_3$: C, 55.47; H, 2.12; N, 11.76. Found: C, 55.03; H, 2.40; N, 12.03.

Other oxazepines did not crystallize, but their structures were confirmed by acceptable UV, mass (existence of the corresponding parent peaks) and NMR spectra (*cf.* Table II). Like IId, these oxazepines also show two absorption maxima above 220 mμ region, respectively: IIa, 252 and 320 mμ; IIb, 248 and 310 mμ; IIc, 234 and 319 mμ.

These crude oxazepines (IIa—c) contain small amounts of parent quinolines (detected by gass-liquid chromatography (GLC) on OV-17), whose amounts (*cf.* Table I) were determined by column chromatography using silica gel after appropriate solvolytic reactions (*vide infra*).

Photolysis of 1-(Trifluoromethyl)isoquinoline 2-Oxide (IV) in Dry Ether——A 500 mg of the N-oxide (IV) was dissolved in dry ether (600 ml). The reaction vessel was protected from moisture by KOH tube and irradiated until all of the N-oxide was consumed (*ca.* 2 hr) in dry argon atmosphere. The solvent was evaporated at room temperature *in vacuo* and the residue was extracted several times with dry pentane. The whole pentane-soluble portion was concentrated below 20° under a reduced pressure. The residue (*ca.* 420 mg) was chromatographed over silica gel with hexane containing 3% of ether to give the oxazepine (V). Yield, 275 mg. UV λ_{max}^{ether} mμ (log ε): 212 (4.60), 300 (3.00). The NMR spectrum is shown in Table II. NMR (CCl_4) τ: 3.22, d (J=8.5 Hz) and 3.44, d (J=8.5 Hz).

22) E. Ochiai, *J. Org. Chem.*, **18**, 534 (1953).
23) Y. Kobayashi, I. Kumadaki, and S. Taguchi, *Chem. Pharm. Bull.*, (Tokyo), **17**, 2335 (1969).

Elution with hexane–ether (9: 1 v/v) gave 35 mg of 1-(trifluoromethyl)isoquinoline.

The longer irradiation resulted in the marked decrease of IV and afforded a new product, whose UV maxima were 214, 274, and 285 mμ. This product was supposed to be the corresponding 2,5-bonded oxazepine,[5] but its definite determination was not made due both to its instability and an insufficient availability of IV.

Irradiation of 2-(Trifluoromethyl)quinoline 1-Oxides (I) in an Alcoholic Medium——The N-oxide (I) in methanol or ethanol was irradiated under the identical conditions as above. Evaporation of the solvent *in vacuo*, column chromatography on silica gel, and crystallization afforded the products (VII and VII'). The yields are given in Table I. The structures of these products were determined by direct comparison with the authentic samples obtained by the solvolytic reactions of the corresponding 3,1-benzoxazepines (II) obtained as above (see, irradiation of I in dry ether).

Irradiation of 1-(Trifluoromethyl)isoquinoline 2-Oxide in Methanol——A 500 mg of the N-oxide (IV) in 500 ml of methanol was irradiated for 2 hr. The solvent was evaporated under a reduced pressure and the residue was chromatographed with silica gel by hexane–ether mixture. 1-(Trifluoromethyl)isoquinoline was obtained from the first fraction. Yield, 35 mg. This was followed by at least three fractions. Among these, only one fraction was successfully crystallized from acetone–hexane (mp 81—83°). Yield, 55 mg. The NMR spectrum (CCl_4) showed a sharp signal at 1.95 due probably to C_3-proton and two broad signals at 1.8 and 2.2 (each corresponded to two protons, respectively), in addition to the methoxy group (5.82, s). *Anal.* Calcd. for $C_{11}H_8ONF_3$: C, 58.15; H, 3.55; N, 6.17. Found: C, 57.93; H, 3.82; N, 6.30.

Action of Methanol (or Ethanol) on 2-(Trifluoromethyl)-3,1-benzoxazepine (IIa) and the Related Compounds (IIb and IId)——The oxazepine (IIa, 325 mg) was dissolved in 50 ml of absolute methanol and the whole solution was stirred for 24 hr at room temperature and then refluxed for 1 hr. Evaporation of the solvent *in vacuo* and subsequent silica gel chromatography with hexane–ether (9: 1 v/v) afforded N-(trifluoromethyl)-dimethoxymethylindole (VIIa, R'=CH_3), 240 mg. Recrystallization form hexane afforded colorless prisms, mp 57—59°. NMR (CCl_4) τ: 2.62, d (1H, J=4 Hz), 3.40, d (1H, J=4 Hz), and 6.42, s (6H). *Anal.* Calcd. for $C_{12}H_{12}O_2NF_3$: C, 55.60; H, 4.67; N, 5.40. Found: C, 55.15; H, 4.74; N, 5.35.

Its structure was further supported by the presence of a typical indole chromophore (λ_{max}^{EtOH} mμ (log ε): 218 (4.60) and 277 (3.70)). It was solvolyzed to indole in an aq. acidic medium.

Further elution by the same solvent gave a trace of indole and 2-(trifluoromethyl)quinoline (20 mg).

The following compounds of VII type were also prepared in essentially the same method; VIIa (R'=CH_2CH_3), mp 29—31°. Yield, from IIa; 46%. UV λ_{max}^{EtOH} mμ (log ε): 276.5 (3.62). NMR ($CDCl_3$)τ: 2.61, d (1H, J=3 Hz), 3.45, d (1H, J=3 Hz), 6.20, q (4H, J=7 Hz), and 8.62, t (6H, J=7 Hz).

VIIb (R'=CH_3), mp 68—70°. Yield, from IIb; 29% (in this case, a substantial amount (39%) of skatol was obtained at the same time). NMR (CCl_4) τ: 2.62, s (1H), 6.43, s (6H), and 7.70, s (3H).

3-Cyanoindole,[24] mp 176—177°, was the only identified product from IId under the identical condition.

Rearrangement of 5-Methoxy-2-(trifluoromethyl)-3,1-benzoxazepine (IIc) in Refluxed Benzene——A 200 mg of IIc in 20 ml of benzene was refluxed for 5 hr. Evaporation of the solvent and recrystallization from acetone afforded 105 mg of 4-methoxy-2-(trifluoromethyl)quinolin-3-ol (XVII), mp 126—128°. NMR ($CDCl_3$) τ: 5.90, s (3H). The same compound was also obtained from IIc in refluxed methanol. *Anal.* Calcd. for $C_{11}H_8O_2NF_3$: C, 54.32; H, 3.32; N, 5.76. Found: C, 53.90; H, 3.53; N, 6.04.

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24) R. Pschor and G. Hoppe, *Ber.*, 43, 2549 (1910).